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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/017,788 | 12/13/2001 | Quan Nguyen | 002558-064310US | 6103 |

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| EXAMINER | |
|---|---|
| COUNTS, GARY W | |
| ART UNIT | PAPER NUMBER |
| 1641 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 01/24/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/017,788 | NGUYEN ET AL. | |
| | Examiner | Art Unit | |
| | Gary W. Counts | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *20-26,28,29,31-52,54,69,70 and 100-102* is/are pending in the application.

4a) Of the above claim(s) *32-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-26,28,29,31,49-52,54,69,70 and 100-102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/30/06 has been entered. Thus, claims 20-26, 28, 29, 31-52, 54, 69, 70 and 100-102 are pending. Claims 32-48 are withdrawn.

### *Claim Rejections - 35 USC § 103*

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 20-26, 28, 29, 31, 49-51 and 100-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oliver et al (Multiplexed Analysis of Human Cytokines by use of the FlowMetrix System, Clinical Chemistry 44, No. 9, 1998) in view of Tamarkin et al (US 5,587,294), Williams et al (US 6,767,708) and Boguslaski et al (US 5,420,016).

Oliver et al disclose methods for the simultaneous quantification of up to 64 different cytokines and also discloses polystyrene microparticles (solid supports) that are differentially stained and produces an array of 64 individually addressable populations of microspheres (p. 2058). Oliver et al disclose the microspheres comprise immobilized capture reagents such as antibodies for the specific cytokines (p. 2058). Oliver et al disclose calibrators (standards) and diluents for the calibrators (p. 2058 & 2059). Oliver et al disclose that the microspheres are incubated with different concentrations of each cytokine. Oliver et al disclose the diluent can comprise serum. Oliver et al disclose fluoresceinated detection reagents. Oliver et al disclose that the anlaytes can be GM-CSF, IL-2, IL-4 and TNF-a. Oliver et al discloses that these microspheres provide for the simultaneous quantitation of cytokines and decreases

assay time from several hours to less than or equal to an hour and also decreases the total amount of sample required and reduces the potential for error because sample splitting is not required (p. 2058). Oliver et al also teaches that the simultaneous analysis of a biological sample for the presence of multiple cytokines will facilitate determining the role of multiple cytokine combinations in disease progression.

Oliver et al differs from the instant invention in failing to teach the standard diluent comprising serum that normally contains the four or more different cytokines but that is substantially free of the four or more different cytokines. Oliver et al also fails to teach packaging the components into a kit.

Tamarkin et al (US 5,587,294) teaches that it is known in the art that serum or plasma comprises cytokines and that the determination of cytokines in biological fluid allows for a clearer picture in disease states (col 8, line 46 – col 9, line 43) and also teaches that serum that has been depleted of cytokines can be used as a diluent (col 16-17)..

Williams et al disclose a method to selectively remove multiple analytes from a biological fluid sample such as serum (col 2, col 4, and col 6). Williams et al teaches that the depleted fluid can be used as a diluent. Williams et al teaches that for both calibrators and controls that it is desirable to use a diluent which displays a behavior in the assay similar to that of the bodily fluid which is to be assayed for the analyte (col 1).

Boguslaski et al disclose assembling various system components into a test kit. Boguslaski et al teaches that by assembling these components into test kits, it makes it more convenient and facile for the test operator (col 7, lines 8-11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate serum as taught by Tamarkin et al into the method of Oliver et al because Oliver specifically teaches that cytokines can be detected in a fluid sample and is generic with respect to the fluid sample. Further, Tamarkin et al teaches that the determination of cytokines in biological fluid such as serum allows for a clearer picture in disease states and Oliver et al teaches that the simultaneous analysis of a biological sample for the presence of multiple cytokines will facilitate determining the role of multiple cytokine combinations in disease progression. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating serum as the fluid sample of Oliver et al.

It would have also been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a diluent that has been depleted of the multiple analytes that are to be detected in an assay such as taught by Williams et al into the modified method of Oliver et al because Williams et al teaches that for both calibrators and controls that it is desirable to use a diluent which displays a behavior in the assay similar to that of the bodily fluid (in this case serum) which is to be assayed for the analyte. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating a depleted diluent into the modified method of Oliver et al.

It would have also been obvious to one of ordinary skill in the art at the time the invention was made to assemble the various reagents and components of the modified method of Oliver et al into a kit because Boguslaski et al shows that packaging these

reagents and components into kits make it more convenient and facile for the test operator.

With respect to the limitations "in which the standard diluent is produced by removing the four or more different cytokines from the biological fluid by affinity chromatography or is obtained from a biological fluid of a host having the biological fluid substantially free of the four or more different cytokines" has not been given patentable weight because the limitations are directed to a product and not a method. The limitations read as a requirement to an assay. Further, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production and if the product in a product by process claim is the same or obvious from a product in the prior art then the claim is unpatentable. Thus the combination of Oliver et al, Tamarkin et al, Williams et al and Boguslaski et al read on the instantly recited claims.

6. Claims 52 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oliver et al in view of Tamarkin et al, Williams et al and Boguslaski et al as applied to claims 20-26, 28, 29, 31, 49-51 and 100-102 above, and further in view of Posner et al (US 4,994,375).

See above for the teachings of Oliver et al., Tamarkin et al., Williams et al., and Boguslaski et al.

Oliver et al., Tamarkin et al., Williams et al., and Boguslaski et al differ from the instant invention in failing to specifically state that the four or more different cytokines are mixed together to form a single concentrated material in part (b).

Posner et al discloses combining different analytes to prepare calibrants and controls (col 2, lines 45-49)(col 3, lines 15-55). Posner et al disclose that the analytes are mixed and lyophilized and stored for later use (col 3, lines 15-68). Posner et al teaches that this control or calibrant is reconstituted by diluent (col 4) and that this provides for means for monitoring of the precision and accuracy of assays (col 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the cytokines as taught by Oliver et al to form a single concentrated material because Posner et al teaches the combination of different analytes to prepare controls or calibrants which are lyophilized and stored for later use and which provide a means for monitoring of the precision and accuracy of assays. Further, one of ordinary skill would recognize that the combination of analytes to form a single concentration material provides for a single control or calibrant that can replace four or more separate control or calibrant products.

With respect to claim 52 as instantly recited. The number of different cytokines as recited in the instant claim. The removal of more than four cytokines different cytokines is viewed as an optimization of the prior art modified method and kit of Oliver et al wherein four different target analytes are removed from a biological fluid to form a diluent. Absent evidence to the contrary the removal of more than four cytokines and the addition of the more than four cytokines to the standard control would merely require adjustment in order to substantially free the biological fluid of the target analytes. Therefore, it would have been obvious to one of ordinary skill in the art to remove more than two different target analytes, since it has long been held that the provision of

adjustability, here needed, involves only routine skill in the art. *In re Stevens,* 101, USPQ 284 (CCPA 1954).

7. Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oliver et al in view of Tamarkin et al., Williams et al., Boguslaski et al and Posner et al as applied to claims 20-26, 28, 29, 31, 49-52 and 100-102 above, and further in view of

See above for teachings of Oliver et al., Tamarkin et al., Williams et al., Boguslaski et al and Posner et al.

Oliver et al., Tamarkin et al., Williams et al., Boguslaski et al and Posner et al. differ from the instant invention in failing to teach eight target analytes are cytokines.

Vignali discloses the detection of IL-6, IL8, IL10 and IFN-y by multiplexed particle-based flow cytometric assays using reagents for the specific analytes (pages 249-250).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate cytokines such as taught by Vignali in the modified method and kit of Oliver et al because Oliver et al teaches that their method can comprise up to 64 different cytokines and Vignali et al disclose that this provides for the simultaneous detection of multiple cytokines which provides the advantage of substantial savings in the cost of reagents and time required to perform the assay. Therefore one of ordinary skill in the art would have a reasonable expectation of success incorporating cytokines such as taught by Vignali into the modified method and kit of Oliver et al.

8. Claim 70 is rejected under 35 U.S.C. 103(a) as being unpatentable over Oliver et al in view of Tamarkin et al., Williams et al and Boguslaski et al as applied to claims 20-26, 28, 29, 31, 49-51 and 100-102 above, and further in view of Foster (US 4,444,879).

See above for the teachings of Oliver et al., Tamarkin et al., Williams et al., and Boguslaski et al.

Oliver et al., Tamarkin et al., Williams et al., and Boguslaski et al differ from the instant invention in failing to teach the kit comprises instructions.

Foster et al disclose packing components and instructions for performing a method into a kit (col 15, lines 11-34).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate instructions as taught by Foster et al into modified method and kit of Oliver et al because Foster et al teaches instructions for performing a method into a kit. Further, the kit would provide guidance and make it more facile and convenient for the test operator.

***Response to Arguments***

9. Applicant's arguments filed 11/30/06 have been considered but are moot in view of the new ground(s) of rejection.

Applicant's arguments directed toward the combination of Williams et al in view of Boguslaski et al. and the combination of Tamarkin et al and Williams et al and further in view of Oliver et al and also the combination of Oliver et al in view of Boguslaski et al are moot in view of the new combination of references applied above.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gary Counts
Examiner
Art Unit 1641
January 17, 2007

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